

Practitioner's Docket No. MPI98-148P1USRCEM

USSN 09/673,302

IN THE CLAIMS:

Please amend the claims as follows:

1. – 68. (Canceled)

69. (Currently Amended) A ~~transgenic~~ chimeric mouse comprising a mutant GP IIIa ( $\beta_3$ ) gene wherein the mutant gene encodes a GP IIIa ( $\beta_3$ ) protein having a conservative amino acid substitution for a wild type tyrosine residue in its mutant cytoplasmic domain ~~tyrosine residue replaced with a non-phosphorylatable residue, wherein said chimeric mouse has reduced or absent phosphorylation of said mutant GP IIIa ( $\beta_3$ ) protein compared to wild type GP IIIa ( $\beta_3$ ) protein.~~

70. (Currently Amended) The ~~transgenic~~ chimeric mouse of claim 69 wherein the mutant cytoplasmic domain tyrosine residue is comprises a conservative amino acid substitution for the wild type tyrosine residue 747 or tyrosine residue 759.

71. (Currently Amended) The ~~transgenic~~ chimeric mouse of claim 69 wherein the non-phosphorylatable residue conservative amino acid substitute in the mutant is phenylalanine.

72. (Currently Amended) A ~~transgenic~~ chimeric mouse comprising a mutant GP IIIa ( $\beta_3$ ) gene wherein the mutant gene encodes a GPIIIa ( $\beta_3$ ) protein having two conservative amino acid substitutions for two wild type tyrosine residues in its

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mutant cytoplasmic domain tyrosine residues replaced with non-phosphorylatable residues.

73. (Currently Amended) The transgenic chimeric mouse of claim 72 wherein the mutant cytoplasmic domain tyrosine residues are comprises conservative amino acid substitutions for the wild type tyrosine residue 747 and tyrosine residue 759.
74. (Currently Amended) The transgenic chimeric mouse of claim 72 wherein each cytoplasmic wild type tyrosine residue is replaced with a substituted by a mutant phenylalanine residue.
75. (Currently Amended) Platelets isolated from blood plasma of the transgenic chimeric mouse of claim 69.
76. (Currently Amended) A transgenic mouse which expresses a transgene integrated into its genome, wherein the transgene comprises DNA encoding a mutant GP IIIa ( $\beta_3$ ) protein having a conservative amino acid substitution for a wild type tyrosine in its mutant cytoplasmic domain tyrosine residue replaced with a non-phosphorylatable residue, wherein said transgenic mouse has reduced or absent phosphorylation of said mutant GP IIIa ( $\beta_3$ ) protein compared to wild type GP IIIa ( $\beta_3$ ) protein.

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77. (Currently Amended) The transgenic mouse of claim 76 wherein the mutant cytoplasmic domain tyrosine residue is comprises a conservative amino acid substitution for the wild type tyrosine residue 747 or tyrosine residue 759.
78. (Currently Amended) The transgenic mouse of claim 76 wherein the non-phosphorylatable residue conservative amino acid substitute in the mutant is phenylalanine.
79. (Currently Amended) A transgenic mouse which expresses a transgene integrated into its genome, wherein the transgene comprises DNA encoding a mutant GP IIIa ( $\beta_3$ ) protein having two conservative amino acid substitutions for two wild type tyrosine residues in its mutant cytoplasmic domain tyrosine residues replaced with non-phosphorylatable residues.
80. (Currently Amended) The transgenic mouse of claim 79 wherein the mutant cytoplasmic domain residues are comprises conservative amino acid substitutions for the wild type tyrosine residue 747 and tyrosine residue 759.
81. (Currently Amended) The transgenic mouse of claim 79 wherein each cytoplasmic wild type tyrosine residue is replaced with a substituted by a mutant phenylalanine residue.
82. (Previously Added) Platelets isolated from blood plasma of the transgenic mouse of claim 76.

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83. (Currently Amended) A method of preparing a transgenic mouse comprising a mutant GP IIIa ( $\beta_3$ ) gene, wherein the mutant gene encodes a mutant GP IIIa ( $\beta_3$ ) protein having a conservative amino acid substitution for a wild type tyrosine in its mutant cytoplasmic domain tyrosine residue replaced with a non-phosphorylatable residue, the method comprising:
- a) introducing into embryonic stem cells a nucleic acid molecule comprising the mutant GP IIIa ( $\beta_3$ ) gene, wherein the mutant gene encodes the mutant GP IIIa ( $\beta_3$ ) protein;
  - b) injecting transformed cells from step a) into one or more blastocysts; and
  - c) generating a transgenic mouse from the cells blastocysts of step [(a)] b).
84. (Currently Amended) The method of claim 83 wherein the mutant cytoplasmic domain tyrosine residue is comprises a conservative amino acid substitution for the wild type tyrosine residue 747 or tyrosine residue 759.
85. (Currently Amended) The method of claim 83 wherein the ~~non-phosphorylatable residue~~ conservative amino acid substitute in the mutant is phenylalanine.
86. (Currently Amended) The method of claim 83 further comprising:
- [[c)] d) mating the transgenic mouse; and
  - [[d)] e) selecting a mouse homozygous for the mutant GP IIIa ( $\beta_3$ ) gene.

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87. (Currently Amended) A method of preparing a transgenic mouse comprising a mutant GP IIIa ( $\beta_3$ ) gene encoding a mutant GP IIIa ( $\beta_3$ ) protein having a conservative amino acid substitution for a wild type tyrosine in its mutant cytoplasmic domain ~~tyrosine residue replaced with a non-phosphorylatable residue~~, the method comprising:
- introducing into embryonic stem cells a nucleic acid molecule comprising the mutant GP IIIa ( $\beta_3$ ) gene encoding the mutant GP IIIa ( $\beta_3$ ) protein and a selectable marker flanked by FRT sites, to produce one or more transformed embryonic stem cells;
  - identifying and selecting the transformed cells;
  - removing the selectable marker from the transformed cells selected in step b) by transient transformation with FLP recombinase;
  - injecting transformed cells from step c) into one or more blastocysts; and
  - generating a transgenic mouse from the blastocysts of step d), wherein the transgenic mouse comprising the mutant GP IIIa gene is heterozygous for the mutant GP IIIa gene.
88. (Currently Amended) The method of claim 87 wherein the ~~non-phosphorylatable residue~~ conservative amino acid substitute in the mutant is phenylalanine.
89. (Currently Amended) The method of claim 87 wherein the mutant cytoplasmic domain ~~tyrosine residue is~~ comprises a conservative amino acid substitution for the wild type tyrosine residue 747 or tyrosine residue 759.

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90. (Previously Added) The method of claim 87 further comprising:

- f) mating the transgenic mouse; and
- g) selecting a transgenic mouse homozygous for the mutant GP IIIa ( $\beta_3$ ) gene.

91. (Previously Added) The method of claim 87 further comprising:

- f) mating a heterozygous transgenic mouse with a second heterozygous transgenic mouse; and
- g) selecting a transgenic mouse homozygous for the mutant GP IIIa ( $\beta_3$ ) gene from the resulting progeny.

92.h) (Currently Amended) A method of determining the effect of an agent on a biological response of the transgenic mouse of claim [[1]] 69, wherein the biological response is mediated by GP IIIa ( $\beta_3$ ) phosphorylation, the method comprising:

- a. administering the agent to the mouse;
- b. determining the effect of the agent on the biological response.

93. (New) A method of determining the effect of an agent on a biological response of the transgenic mouse of claim 76, wherein the biological response is mediated by GP IIIa ( $\beta_3$ ) phosphorylation, the method comprising:

- c. administering the agent to the mouse;
- d. determining the effect of the agent on the biological response.